natural amino acid residue substitutes thereof, the C-terminus carboxamides thereof, the C-terminus esters thereof, the D-terminus ketones thereof, the N-terminus modifications thereof, or any mixture thereof.

44. (twice amended) A method of enhancing metabolism of nutrients, comprising administering by a parenteral route to a patient in need of enhancing metabolism of nutrients a nutritively effective composition comprising glucose and one or more insulinotropic peptide or peptides, wherein said insulinotropic peptide or peptides is GLP-1, GLP-1 (7-34), GLP-1(7-35), GLP-1 (7-36), GLP (7-37), the deletion sequences thereof, the natural and non-natural amino acid residue substitutes thereof, the C-terminus carboxamides thereof, the C-terminus esters thereof, the D-terminus ketones thereof, the N-terminus modifications thereof, or any mixture thereof.

REMARKS

Claims 1, 2, 17-26, 28-39, and 41-50 are pending in the application. Claims 26, 28-31, and 36-39 have been withdrawn with traverse as to a non-elected invention. Claims 41 and 44 have been amended without prejudice or disclaimer of any subject matter.

Formal matters:

Applicants again respectfully request acknowledgement of the claim for foreign priority under 35 U.S.C. § 119 to DE 19530865.4, filed August 22, 1995, and of receipt by the Patent and Trademark Office of the certified copy of the same.

Rejections under 35 USC § 112, first paragraph (support for claimed subject matter):

Claims 20, 21, 41, and 44 and claims dependent thereon are rejected under 35 USC § 112, first paragraph, as inadequately described by the specification. Applicants traverse the rejections.

[A] The Examiner alleges that claim 21 introduces new matter insofar as it encompasses modes of administration other than infusion. Claim 21 as originally filed prescribes "administration." Since this term was never added by amendment, its retention cannot now

predicate a rejection for introducing matter unsupported by the specification. Further, the specification repeatedly describes "administration" of the compositions of the invention, not just their "infusion," thereby providing adequate written support for the term. Indeed, infusion is only one of many modes of administration contemplated by the invention, which are exemplified at page 6, lines 15-21. The rejection is improper and should be withdrawn.

[B] The amendment introducing "organic molecular mimics of the insulinotropic peptides which fit the insulinotropic receptor sites" into claims 41 and 44 allegedly introduces new matter. Applicants maintain that this claim is supported by the specification. The term is deleted to expedite prosecution, rendering the rejection moot, but the amendment does not constitute acquiescence to the Examiner's rejection.

[C] Claim 20 allegedly introduces new matter in connection with meaning of the term "nutrients." Claim 20 was not amended in the Response filed December 1, 2000, so it is impossible that the claim now be the subject of a rejection for introducing subject matter unsupported by the specification. The rejection cannot be sustained because it has no legal basis. Moreover, support is found for this claim term throughout the specification. See for example, pages 2, 4, or 6.

Rejections under 35 USC § 112, second paragraph:

Claims 20, 41, and 44 and claims dependent thereon are rejected under 35 USC § 112, second paragraph, for indefiniteness. Applicants traverse the rejections.

[A] Claim 20 allegedly is unclear because "the source of carbohydrate nutrients" lacks antecedent basis. This term was removed from the claim in the Response filed March 9, 2000, so the rejection is moot.

Claim 20 currently recites:

> 20. (Amended) The method of claim 1 wherein the administration of the nutrient to the patient produces a blood glucose level in the patient of from about 80 to 180 mg glucose per deciliter of blood and the rate of administration of the source of carbohydrate nutrients is calculated to deliver up to about 1000 g of glucose or its equivalent per patient per day.

This recitation is provided solely for the Examiner's reference and does not constitute a clean copy of the claim, for the purpose of 37 CFR § 1.121.

[B] Claims 41 and 44 are rejected because "organic molecular mimics" allegedly does not set forth the metes and bounds of the term. Applicants maintain that this term is not indefinite. The term is deleted, rendering the rejection moot, but the amendment does not constitute acquiescence to the Examiner's rejection.

Rejections under 35 USC § 112, first paragraph (written description and enablement):

Claims 41 and 44 and their dependents are rejected under 35 USC § 112, first paragraph, with respect to the claim term "organic molecular mimics" for being based on a disclosure that allegedly provides inadequate written description, fails to disclose essential subject matter, and does not enable the practice of the invention. Applicants maintain that the claimed invention is enabled and that "organic molecular mimics" are adequately described; nevertheless, the rejections are moot in view of the claim amendment.

Rejections under 35 USC § 102:

I. Claims 1-2, 17-19, 21-25, 32-35, and 40-48 are rejected under 35 USC § 102(b), as anticipated by U.S. Pat. No. 5,118,666 to Habener (" '666 patent"). Applicants traverse the rejection.

In the response and amendment filed December 1, 2000, applicants stated that the rejection was improper because (1) the '666 patent nowhere teaches administration of a composition comprising an insulinotropic compound by a parenteral route to a patient in need of parenteral nutrition, and (2) it nowhere teaches, or even suggests, parenteral administration of a composition that provides an effective amount of nutrients to a patient in need of nutrition. In response, the Examiner points to Example 9, where Habener discusses perfusion of a rat pancreas with a composition comprising an insulinotropic compound and glucose.

To anticipate properly the claimed invention, the '666 patent must teach at least administration by a parenteral route in a manner embraced by the claimed method; however, the mode of administration used by Habener in example 9 is not embraced by the claims. Habener uses a "rat pancreas perfusion system" (col. 17, line 48), which is described at

column 13, lines 50-52, with reference to Weir *et al.* (1974) *J. Clin. Invest.* 54:1403-1412 and Penkos *et al.* (1969) *Diabetes* 18: 733-738. These articles are attached as Exhibits A and B. Weir and Penkos evidence that the rat pancreas perfusion method requires the excision of the pancreas from the rat and the injection of an insulinotropic agent into the isolated pancreas. As such, this method prescribes the *ex vivo* administration of the insulinotropic agent.

By contrast, the insulinotropic composition in the claimed method is administered to a patient in need of parenteral nutrition. This population of patients reasonably excludes those whose organs are first removed and then treated with an insulinotropic agent, according to the procedure defined in the '666 patent. Applicants may interpret claim terms during prosecution to clarify the meaning of the claims, and the claims must then be examined according to that meaning. *In re Zletz*, 893 F.2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989). Applicants have clarified that the claims exclude the injection of an insulinotropic agent into an organ *ex vivo*, as taught by the '666 patent. The '666 patent does not teach administration to a patient in need of parenteral nutrition; accordingly, it does not anticipate the claimed invention, and the rejection should be withdrawn.

II. Claims 1-2, 17-19, 21-25, 32-35, and 40-48 are rejected under 35 USC §§ 102(b) and (e), as anticipated by U.S. Pat. No. 5,614,492 to Habener (" '492 patent"). Applicants traverse the rejection.

In the response and amendment filed December 1, 2000, applicants stated that the rejection was improper because (1) the '492 patent teaches parenteral administration of an insulinotropic agent only at column 9, but that (2) this agent is not administered in the presence of a nutritively effective amount of a nutrient. The Examiner does not disagree with these assertions, but alleges that applicants are not considering the reference as a whole.

Applicants have considered the '492 patent's teachings as a whole, and they believe that their response filed December 1st constitutes a full and complete response to the rejection. As applicants pointed out in the December 1st response, the '492 patent does not teach *parenteral* administration of an insulinotropic agent with a nutritively effective amount of a nutrient. The passages referred to by the Examiner teach *non-parenteral* administration of a composition comprising an insulinoptropic agent and nutrients. Stedman's Medical

Dictionary, 23rd ed., defines "parenteral" as "by some other means than through the intestinal canal, referring particularly to the introduction of nutritive material into veins and subcutaneous tissue." Except for the passage at column 9 that applicants discuss above, the passages cited by the Examiner teach oral ingestion of the insulinotropic agent or nutrients. In particular, Example 11 does not teach *parenteral* administration of a composition comprising an insulinotropic agent and nutrients. Column 22, lines 52-67 describe the injection (parenteral administration) of an insulinotropic agent to subjects, but the nutrients delivered to these same subjects are delivered *non-parenterally*. The study is preformed with subjects having "a standard breakfast meal **consumed** during the first 15-20 minutes of the GLP infusion" (emphasis added; parenthetical material omitted). Column 22, line 63. The claimed method, however, prescribes that the insulinotropic agent and nutrients are **both** delivered parenterally. Accordingly, the '492 patent also does not anticipate the claimed invention, and the rejection should be withdrawn.

Rejection under 35 USC § 103:

Claims 1-2, 17-25, 32-35, and 40-50 are rejected under 35 USC § 103(a), as obvious over "the specification disclosure as to the state of the prior art" in view of the '492 patent "and/or" U.S. Pat. No. 5,424,286 ("Eng").

In the response and amendment filed December 1, 2000, applicants stated that (1) Eng does not make up for the deficiencies of the '492 patent, because Eng teaches administration of insulinotropic compounds attached to carrier molecules that are not delivered in nutritively effective amounts, and (2) Eng teaches away from the claimed invention, because he suggests removing the very compounds from the insulinotropic compound that the Examiner identifies as "nutrients." Further, as applicants have stated previously, the '492 patent likewise teaches away from the invention, where it describes the very compounds the Examiner alleges are contained in a composition with an insulinotropic compound as "contaminants" (column 9, line 25). Thus, the cited references suggest **removing** nutrients from a parenterally administered composition comprising the insulinotropic agent. They do not suggest parenteral administration of a composition comprising **both** an insulinotropic agent and a nutritively effective amount of a nutrient, as claimed.

In response, the Examiner again alleges that applicants have failed to address the references as a whole. The Examiner points with particularity to Examples 9 and 11 of the '492 patent. Example 9 of the '492 patent employs the same rat pancreas assay that was used in Example 9 of the '666 patent. See the '492 patent at column 19, line 50 and column 15, lines 60-66. Applicants have addressed this assay above and have stated that it is dissimilar to the present mode of administration and that it is not encompassed by the present claims. Applicants have addressed Example 11 above and have stated that this example does not disclose the parenteral administration of an insulinotropic agent and a nutritively effective amount of a nutrient, as claimed. Applicants again believe that they have addressed these references as a whole.

The Examiner finally alleges that applicant "has failed to address the teaching of the specification with the above Eng and Habener references." The meaning of this allegation is unclear. If the Examiner wishes to raise a new line of rejection, applicants will respond duly and completely.

It is axiomatic that a proper rejection for obviousness must point out those teachings of the cited references that, when combined, suggest each and every element of the claimed invention. In the present rejection, neither Eng nor Habener teach or suggest the claimed element of parenteral administration of a composition comprising an insulinotropic agent and a nutritively effective amount of a nutrient, for the reasons stated above. It is the combined parenteral administration of these two components that provides the advantage of the invention. Traditional nutritional therapies use a low rate of parenteral nutrient administration so that the blood sugar level does not exceed normal physiological limits; however, when the presently claimed method is used, the requisite nutrients may be delivered parenterally while maintaining an appropriate blood sugar level. See the specification at page 2, for example. This advantage is provided by the present specification, not the cited art. Insofar as the rejection relies on the artisan of ordinary skill possessing this insight at the time of the invention, the rejection is predicated improperly on hindsight provided by applicants' disclosure. The rejection thus should now be withdrawn.

CONCLUSION

In view of the foregoing, it is respectfully urged that the present claims are in condition for allowance. An early notice to this effect is earnestly solicited. Should there be any questions regarding this application, the examiner is invited to contact the undersigned at the telephone number shown below.

Respectfully submitted,

June 20, 2001
Date

Brian Lathrop
Brian K. Lathrop
Agent for Applicants
Registration No. 43,740

FOLEY & LARDNER
3000 K Street, N.W., Suite 500
Washington, D.C. 20007
Phone: (202) 672-5300
Fax: (202) 672-5399

Marked-up version of the amended claims

41. (twice amended) A method of enhancing metabolism of nutrients, comprising administering by a parenteral route to a non-diabetic patient in need of enhancing metabolism of nutrients a nutritively effective composition comprising one or more nutrients or any combination thereof and one or more insulinotropic peptide or peptides, wherein said peptide or peptides is GLP-1, GLP-1 (7-34), GLP-1(7-35), GLP-1 (7-36), GLP (7-37), the deletion sequences thereof, the natural and non-natural amino acid residue substitutes thereof, the C-terminus carboxamides thereof, the C-terminus esters thereof, the D-terminus ketones thereof, the N-terminus modifications thereof**[, organic molecular mimics of the insulinotropic peptides which fit the insulinotropic receptor sites]**, or any mixture thereof.

44. (twice amended) A method of enhancing metabolism of nutrients, comprising administering by a parenteral route to a patient in need of enhancing metabolism of nutrients a nutritively effective composition comprising glucose and one or more insulinotropic peptide or peptides, wherein said insulinotropic peptide or peptides is GLP-1, GLP-1 (7-34), GLP-1(7-35), GLP-1 (7-36), GLP (7-37), the deletion sequences thereof, the natural and non-natural amino acid residue substitutes thereof, the C-terminus carboxamides thereof, the C-terminus esters thereof, the D-terminus ketones thereof, the N-terminus modifications thereof**[, organic molecular mimics of the insulinotropic peptides which fit the insulinotropic receptor sites]**, or any mixture thereof.